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cont

an inner layer of a cationic polyelectrolyte carrier; and  
a layer of at least one negatively charged therapeutic agent adsorbed onto said inner layer  
of cationic polyelectrolyte carrier; and  
an additional layer or layers of cationic polyelectrolyte carrier and an additional layer or  
layers of at least one negatively charged therapeutic agent adsorbed onto said additional  
layer or layers of cationic polyelectrolyte carrier, wherein said additional layer or layers  
of polyelectrolyte carrier and said additional layer or layers of negatively charged  
therapeutic agent alternate.

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6.<sup>11</sup> The medical device of claim 1, wherein at least one of the one or more negatively charged  
therapeutic agent comprises at least one agent selected from the group consisting of anti-  
thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of  
blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers,  
antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic  
agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth  
inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with  
endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors,  
anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and  
polynucleotides encoding such agents.

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15.<sup>11</sup> The method of claim 10, wherein at least one of the one or more negatively charged  
therapeutic agent comprises at least one agent selected from the group consisting of anti-  
thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of  
blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers,  
antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic  
agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth  
inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with  
endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors,

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cont anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

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A4 24. <sup>AMENDED</sup> The medical device of claim 19, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

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28.<sup>11</sup> A method of delivering a therapeutic agent to a target location by implanting in [or near] the target location in a mammal a medical device comprising a negatively charged therapeutic agent adsorbed on the surface thereof; wherein the medical device is produced by a process comprising:

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- (a) coating at least one portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
  - (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
  - (c) adsorbing one or more negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
  - (d) washing the layer of therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

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<sup>AMENDED</sup>  
33. The method of claim 28, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

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37.<sup>22</sup> The method of claim 28, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

38.<sup>21</sup> A method for treating or reducing the occurrence or severity of a clinical disease or condition, comprising:

A7 (a) preparing a medical device by:

- (i) coating at least one portion of at least one surface a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing one or more negatively charged therapeutic agent effective to treat or reduce the occurrence of the clinical disease or condition onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic

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polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into a target location in a mammal from which the therapeutic agent can treat or reduce the occurrence or severity of the clinical disease or condition.

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43. <sup>AMENDED</sup> The method of claim 38, wherein at least one of the one or more negatively charged therapeutic agent comprises at least one agent selected from the group consisting of anti-thrombogenic agents, antioxidants, angiogenic agents, anti-angiogenic agents, agents capable of blocking smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic agents, antiproliferative agents, anti-mitotic agents, anti-microbials, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoters, vascular cell growth inhibitors, cholesterol lowering agents, vasodilating agents, agents which interfere with endogenous vasoactive mechanisms, agents that protect against cell death, cell cycle inhibitors, anti-restenosis agents, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding such agents.

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46. The method of claim 38, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

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Please add the following new claims:

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47. The medical device of claim 1 wherein at least one of the one or more therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which block smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-

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microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding any of the above named proteins.

<sup>39</sup>  
~~48~~. The medical device of claim 47 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

49. The medical device of claim 47 wherein the antioxidant compounds is probucol or retinoic acid.

<sup>40</sup>  
~~50~~. The method of claim 10 wherein at least one of the one or more therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which block smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding any of the above named proteins.

<sup>42</sup> <sup>41</sup>  
~~51~~. The method of claim ~~50~~ wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

52. The method of claim 50 wherein the antioxidant compounds is probucol or retinoic acid.

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53. The method of claim 19 wherein at least one of the one or more therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which block smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding any of the above named proteins.

54. The method of claim 53 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

55. The method of claim 53 wherein the antioxidant compounds is probucol or retinoic acid.

56. The method of claim 28 wherein at least one of the one or more therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which block smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding any of the above named proteins.

57. The method of claim 56 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

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58. The method of claim 56 wherein the antioxidant compounds is probucol or retinoic acid.

59. The method of claim 38 wherein at least one of the one or more therapeutic agents is selected from the group consisting of: anti-thrombogenic proteins, antioxidant compounds, angiogenic proteins, agents which block smooth muscle cell proliferation, anti-inflammatory agents, calcium entry blockers, antineoplastic/antiproliferative/anti-mitotic compounds, anti-microbial compounds, anesthetic agents, nitric oxide donors, anti-coagulants, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, vascular cell growth antibody inhibitors, cholesterol lowering drugs, vasodilating drugs, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, agents for treating malignancies, bone morphogenic proteins, and polynucleotides encoding any of the above named proteins.

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60. The method of claim <sup>50</sup>59 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

61. The method of claim 59 wherein the antioxidant compounds is probucol or retinoic acid.

62. A method of delivering a therapeutic agent to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is produced by a process comprising:

- (a) coating at least one portion of at least one surface of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (b) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (c) adsorbing one or more negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (d) washing the layer of therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier

and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

63. A method of delivering a DNA encoding a protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

- (i) coating at least one portion of at least one surface of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing one or more negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device; wherein at least one of the one or more negatively charged therapeutic agents is the DNA encoding a protein.

64. A method of delivering a DNA encoding a therapeutic protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

- (i) coating at least one portion of at least one surface of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
- (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
- (iii) adsorbing one or more negatively charged therapeutic agents onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
- (iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto



the medical device; wherein at least one of the one or more negatively charged therapeutic agents is the DNA encoding a therapeutic protein, wherein the therapeutic protein is selected from the group consisting of anti-thrombogenic proteins, angiogenic proteins, vascular cell growth promoting proteins, vascular cell growth protein inhibitors, proteins that protect against cell death, cell cycle CDK protein inhibitors, anti-restenosis proteins, and bone morphogenic proteins.

65. A method for inhibiting restenosis or the growth of tumor cells in a mammal, comprising:
- (a) preparing a medical device by:
    - (i) coating at least one portion of at least one surface of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;
    - (ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;
    - (iii) adsorbing one or more negatively charged therapeutic agents effective to inhibit restenosis or the growth of tumor cells onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally
    - (iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device;
  - (b) implanting the medical device into a target location in a mammal;
- wherein at least one of the one or more negatively charged therapeutic agents is a DNA coding for an anti-proliferative protein.

66. A method for inducing the growth of blood vessels at a target location in a mammal, comprising:

- (a) preparing a medical device by:
  - (i) coating at least one portion of at least one surface of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

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(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;  
(iii) adsorbing one or more negatively charged therapeutic agents effective to induce the growth of blood vessels onto the layer of cationic polyelectrolyte carrier to form a layer of therapeutic agent; and optionally  
(iv) washing the layer of therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and therapeutic agent until a desired amount of therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into the target location in a mammal;  
wherein at least one of the one or more negatively charged therapeutic agents is a DNA coding for an angiogenic protein.

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